

### **REMARKS/ARGUMENTS**

Claims 1-49 are pending in the above-identified application. Claim 1 is allowed and Claims 2-49 are rejected. In this response: a) claims 2, 3, and 6-49 are canceled without prejudice; b) claims 4 and 5 are amended; c) claims 50-87 are added; and d) the following remarks/arguments are presented for consideration by the Examiner. The instant amendment to the claims is made to more clearly define the present invention and not to avoid cited art. No new matter is added to either the specification or claims with this response and/or amendment.

Applicants contend one of ordinary skill in the art will understand and find general support or antecedent basis for new Claims 50-73 throughout the instant specification, but more specifically as follows: 1) original Claims 6-10 and 41-42; 2) page 5, paragraph 11; 3) page 9, paragraph 21; and 4) page 13, paragraph 33 through page 15, paragraph 38.

Applicants additionally contend one of ordinary skill in the art will understand and find general support or antecedent basis for new Claims 74-79 throughout the instant specification, but more specifically as follows: 1) original Claims 11-14 and 43-45; 2) page 5, paragraph 11; 3) page 17, paragraph 42; 4) page 18, paragraph 44; 5) page 20, paragraph 48 through page 25, paragraph 56.

Applicants further contend one of ordinary skill in the art will understand and find general support or antecedent basis for new Claims 80-87 throughout the instant specification, but more specifically as follows: 1) original Claims 15-35 and 46-49; 2) page 4, paragraph 10; 3) page 5, paragraph 12 through page 6, paragraph 14; 4) page 13, paragraph 33; 5) page 15, paragraph 38; 6) page 16, paragraph 41 through page 31, paragraph 69.

Applicants respectfully request consideration of the following remarks and entry of the above amendment into the official record of the instant application. Claim 1 (is allowed) and Claims 4, 5, and 50-87 are now pending. Applicants respectfully request that the instant pending claims 4, 5, and 50-87 be duly allowed.

#### **Oath or Declaration**

Applicants acknowledge the Examiner's objection to the oath or declaration submitted in the instant application. The oath or declaration is not necessary to further consideration of the pending claims and Applicants respectfully request this requirement be held in abeyance until instant pending claims 4, 5, and 50-87 are deemed allowable by the Examiner. A new oath or declaration will be submitted prior to payment of the issue fee.

### **Claim Objections**

Claims 9, 12, 16, 41, and 44 are objected to by the Examiner because the word “complementary” is misspelled. Additionally, Claims 41 and 44 are objected to by the Examiner because the phrase “is of at least” is not proper English.

With regard to the Examiner’s objection to the misspelling of the word “complementary”, Applicants acknowledge the typographical error. However, the Examiner’s objection is made moot by the instant amendment to Claims 9, 12, 16, 41, and 44.

With regard to the Examiner’s objection to the phrase “is of at least” in Claims 41 and 44, Applicants respectfully remind the Examiner that there is no official requirement that the specification or claims be written in “proper” English. According to 35 U.S.C. 112, second paragraph, the claims only need to meet the threshold of clarity and precision, not whether more suitable language or modes of expression are available. Further, M.P.E.P § 2173.02 states “Some latitude in the manner of expression and the aptness of terms should be permitted even though the claim language is not as precise as the Examiner might desire”. That said, the Examiner’s objection is made moot by the instant amendment to Claims 41 and 44.

### **Rejection under 35 U.S.C. § 112, second paragraph**

Claims 6-49 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner has rejected specific claims under 35 U.S.C. § 112, second paragraph, as follows:

- (i) *Claim 6 is indefinite due to the recitation “antisense cDNA”;*
- (ii) *Claim 7 is indefinite due to the recitation “antisense cDNA”;*
- (iii) *Claim 8 (and dependent Claims 9, 10, and 36-40) is indefinite due to the recitation “derived from”;*
- (iv) *Claim 9 (and dependent Claims 10 and 36-40) is indefinite due to the recitation “low and high stringency conditions”;*
- (v) *Claim 11 (and dependent Claims 12-14) is indefinite due to the recitation “effective amount”;*
- (vi) *Claim 11 (and dependent Claims 12-14) is indefinite due to the recitation “derived from”;*
- (vii) *Claim 13 is indefinite due to the recitation “low and high stringency conditions”;*

- (viii) Claim 15 (and dependent Claims 16-21) is indefinite due to the recitation "derived from";*
- (ix) Claim 15 (and dependent Claims 16-21) is indefinite due to the recitation "excess of tubedown-1 gene";*
- (x) Claim 15 (and dependent Claims 16-21) is indefinite due to the recitation "biologically active";*
- (xi) Claim 17 (and dependent Claims 18-21) is indefinite due to the recitation "low and high stringency conditions";*
- (xii) Claim 20 is indefinite because it recites an improper Markush group;*
- (xiii) Claim 20 is indefinite due to the recitation "virus-like vectors";*
- (xiv) Claim 22 (and dependent Claims 23-27) is indefinite due to the recitation "said condition" lacks antecedent basis;*
- (xv) Claim 22 (and dependent Claims 23-27) is indefinite due to the recitation "derived from";*
- (xvi) Claim 24 (and dependent Claim 25) is indefinite because it is unclear what is meant by the phrase "generated ex-vivo" and how it relates to Claim 23;*
- (xvii) Claim 25 is indefinite because the antecedent basis for "the antisense cDNA's" is unclear;*
- (xviii) Claim 25 is indefinite because it is unclear how the antisense can be phosphoramidate, phosphorothioate, methylphosphonate, and other modified analogs;*
- (xix) Claim 25 is indefinite because the scope of "other modified analogs of said cDNA" is unclear;*
- (xx) Claim 26 (and dependent Claim 27) is indefinite because it is unclear how the method of Claims 26 and 23 are related;*
- (xxi) Claim 28 (and dependent Claims 29-33) is indefinite due to the recitation "derived from";*
- (xxii) Claim 28 (and dependent Claims 29-33) is indefinite due to the recitation "said condition" lacks antecedent basis;*

- (xxiii) Claim 30 (and dependent Claim 31) is indefinite because it is unclear what is meant by the phrase "generated ex-vivo" and how it relates to Claims 28 and 29;*
- (xxiv) Claim 30 (and dependent Claim 31) is indefinite because the antecedent basis for "the antisense oligonucleotide" is unclear;*
- (xxv) Claim 31 is indefinite because the antecedent basis for "the antisense cDNA molecules" is unclear;*
- (xxvi) Claim 31 is indefinite because it is unclear how the antisense can be phosphoramidate, phosphorothioate, methylphosphonate, and other modified analogs;*
- (xxvii) Claim 31 is indefinite because the scope of "other modified analogs of said cDNA" is unclear;*
- (xxviii) Claim 32 (and dependent Claim 33) is indefinite because the antecedent basis for "the antisense cDNA's" is unclear;*
- (xxix) Claim 32 (and dependent Claim 33) is indefinite because it is unclear how the method of Claims 32 and 29 are related;*
- (xxx) Claim 34 is indefinite due to the recitation "said tbdn-1 protein" lacks antecedent basis;*
- (xxxi) Claim 35 is indefinite due to the recitation "said tbdn-1 protein" lacks antecedent basis;*
- (xxxii) Claim 41 (and dependent Claim 42) is indefinite due to the recitation "derived from";*
- (xxxiii) Claim 46 (and dependent Claims 47 and 48) is indefinite due to the recitation "derived from";*
- (xxxiv) Claim 47 (and dependent Claim 48) is indefinite because the antecedent basis for "the antisense oligonucleotide" is unclear;*
- (xxxv) Claim 47 (and dependent Claim 48) is indefinite because it is unclear how the antisense can be phosphoramidate, phosphorothioate, methylphosphonate, and other modified analogs;*
- (xxxvi) Claim 47 (and dependent Claim 48) is indefinite because the scope of "other modified analogs of said cDNA molecules" is unclear;*

*(xxxvii) Claim 48 is indefinite because it is unclear what is meant by the phrase "generated ex-vivo" and how it relates to Claims 46 and 47;*

*(xxxviii) Claim 49 is indefinite due to the recitation "derived from";*

*(xxxix) Claim 49 is indefinite due to the recitation "said condition" lacks antecedent basis.*

In view of the instant amendment wherein Applicants have canceled the above-identified claims, and therefore rendered the above rejections inapplicable, Applicants do not wish to further burden the Examiner by needlessly replying herein to each of the above thirty-nine rejections individually. Suffice it to say that, Applicants have thoughtfully considered the Examiner's comments and believe that one of ordinary skill in the relevant art would understand the language of the claims as originally written and be able to interpret the claims appropriately. The instant amendment to the claims is made to more clearly define the present invention and not to avoid the Examiner's rejections.

That said, Applicants respectfully request the Examiner withdraw the above rejections under 35 U.S.C. § 112, second paragraph, consider the "new" claims presented herein for examination, and duly allow all the instantly pending claims, i.e., Claims 4, 5, and 50-87. Applicants believe these "new" claims more clearly reflect the present invention and that the Examiner will find them acceptable under 35 U.S.C. § 112, second paragraph. Full support for these "new" claims may be found throughout the entire specification.

**Rejection under 35 U.S.C. § 112, first paragraph**

Claims 2-5, 8, 11-13, 15-17, 19-22, 24-28, 30-35, and 41-49 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 15-33, and 46-49 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Like Applicants response above to the Examiner's rejections under 35 U.S.C. § 112, second paragraph, the above-identified claims have been canceled by the instant amendment, and therefore rendered the above rejections inapplicable. Therefore, to avoid further burdening the Examiner by needlessly replying herein to each of the above rejections under 35 U.S.C. § 112, first paragraph, Applicants respectfully request the Examiner withdraw the above rejections

under 35 U.S.C. § 112, first paragraph, consider the “new” claims presented herein for examination, and duly allow all the instantly pending claims, i.e., Claims 4, 5, and 50-87. Applicants believe these “new” claims more clearly reflect the present invention and that the Examiner will find them acceptable under 35 U.S.C. § 112, first paragraph. Full support for these “new” claims may be found throughout the entire specification.

### **Conclusion**

Applicants respectfully request the Examiner enter this response, in view of the instant amendment and “new” claims added to the instant application, into the record of the instant application as a *bona fide* response. Applicants have amended their claims to more clearly define the instant invention and not to avoid cited art or the Examiner’s rejections. Applicants believe that each of the rejections under 35 U.S.C. § 112, first and second paragraphs, have been overcome.


WHEREFORE, reconsideration of this application, in view of the foregoing amendment and remarks, Applicants respectfully request the objections and rejections be withdrawn and all the instant pending claims, claims 1, 4, 5, and 50-87, be duly allowed.

The Examiner is encouraged by Applicants to contact Applicants’ representative at the telephone number shown below with any comments/questions regarding this response. Other issues related to this application should be directed to Applicant’s Attorney/Agent of record.

Respectfully submitted for,

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## VERSION OF CLAIMS WITH MARKINGS TO SHOW CHANGES MADE

Deletions to the claims are indicated by ~~striketrough~~ and additions are indicated by **bold type and underlining** the added matter.

Claim 1 is unchanged:

1. An isolated nucleic acid molecule consisting of the sequence shown in SEQ ID No. 2.

Claim 2 is deleted:

- ~~2) An isolated nucleic acid molecule which encodes a protein comprising an amino acid sequence at least 70 % homologous to the amino acid sequence of SEQ ID No. 1, wherein said amino acid sequence is expressed in bone tumors.~~

Claim 3 is deleted:

- ~~3) The isolated nucleic acid molecule of Claim 2, comprising the nucleotide sequence of SEQ ID No. 2.~~

Claim 4 is amended as follows:

4. (Amended) The isolated nucleic acid molecule of Claim ~~3~~1, wherein ~~the amino acid sequence~~ **said molecule** is expressed in Ewing's Sarcoma family of tumors.

Claim 5 is amended as follows:

5. (Amended) The isolated nucleic acid molecule of Claim ~~3~~1, wherein ~~the amino acid sequence~~ **said molecule** is expressed in osteosarcoma tumors.

Claim 6 is deleted:

- ~~6) An antisense cDNA molecule consisting of the sequence shown in SEQ ID No. 3.~~

Claim 7 is deleted:

- ~~7) An antisense cDNA molecule consisting of the sequence shown in SEQ ID No. 4.~~

Claim 8 is deleted:

- ~~8) An antisense cDNA molecule derived from a cDNA sequence of SEQ ID NO. 2, wherein the antisense cDNA molecule is at least 1000 nucleobases in length and produces an antisense mRNA, wherein said antisense mRNA is at least 70% complementarity to native mRNA produced by a tubedown-1 gene.~~

Claim 9 is deleted:

- ~~9) The antisense cDNA molecule of claim 8, wherein the antisense mRNA and native mRNA hybridize under low and high stringency conditions.~~

Claim 10 is deleted:

- ~~10) The antisense cDNA molecule of claim 9, wherein the antisense cDNA molecule is selected from the group consisting of SEQ ID NO. 3 and SEQ ID NO. 4.~~

Claim 11 is deleted:

- ~~11) A composition comprising a safe and effective amount of an antisense cDNA molecule derived from a cDNA sequence of SEQ ID NO. 2, and a pharmaceutically acceptable carrier.~~

Claim 12 is deleted:

- ~~12) The composition of claim 11 wherein the antisense cDNA molecule is at least 1000 nucleobases in length, and wherein the antisense cDNA produces an antisense mRNA which is at least 70% complementarity to an mRNA produced by a native tubedown-1 gene.~~

Claim 13 is deleted:

- ~~13) The composition of claim 12 wherein the antisense mRNA and native mRNA hybridize under low and high stringency conditions.~~

Claim 14 is deleted:

- ~~14) The composition of claim 13 wherein the antisense cDNA is selected from the group consisting of SEQ ID NO. 3 and SEQ ID NO. 4.~~

Claim 15 is deleted:

- ~~15) A method of providing biologically active antisense cDNA derived from a cDNA sequence of SEQ ID NO. 2, to cells of an individual producing excess of a tubedown-1 gene, said method comprising in vivo administration into cells a vector comprising and expressing the antisense cDNA which produces an antisense mRNA, which binds to native mRNA produced by the tubedown-1 gene, thereby blocking expression of said gene.~~

Claim 16 is deleted:

- ~~16) The method of claim 15 wherein the antisense cDNA molecule generates antisense mRNA of at least 70% complementarity to mRNA produced by a native tubedown-1 gene.~~

Claim 17 is deleted:

- ~~17) The method of claim 16 wherein the antisense mRNA and native mRNA hybridize under low and high stringency conditions.~~



Claim 18 is deleted:

~~18) The method of claim 17 wherein the antisense cDNA molecule is selected from the group consisting of SEQ ID NO. 3 and SEQ ID NO. 4.~~

Claim 19 is deleted:

~~19) The method of claim 17 wherein the vector is a viral vector.~~

Claim 20 is deleted:

~~20) The method of claim 19 wherein the viral vector is selected from the group consisting of a lentivirus, adenovirus, adeno-associated virus and virus-like vectors.~~

Claim 21 is deleted:

~~21) The method of claim 17 wherein the vector is a plasmid.~~

Claim 22 is deleted:

~~22) A method for treatment of osteosarcoma in a mammal, said method comprising administering to said mammal a safe and effective amount of an antisense cDNA molecule derived from a cDNA molecule of SEQ ID NO. 2 sufficient to treat said condition.~~

Claim 23 is deleted:

~~23) The method of claim 22, wherein the antisense cDNA molecule is selected from the group consisting of SEQ ID NO. 3 and SEQ ID NO. 4 and mixtures thereof.~~

Claim 24 is deleted:

~~24) The method of claim 23 wherein said method further comprises generation of the antisense cDNA ex vivo which, when introduced into the cell, causes inhibition of expression of a tubedown-1 protein by hybridizing with mRNA and genomic sequences of a tbdn-1 gene.~~

Claim 25 is deleted:

~~25) The method of claim 24 wherein the antisense cDNA's are phosphoramidate, phosphothioate, methylphosphonate and other modified analogs of said cDNA which are resistant to endogenous nucleases.~~

Claim 26 is deleted:

~~26) The method of claim 23, wherein said method further comprises providing the antisense cDNA to cells of an individual expressing a tubedown-1 protein, said method comprising in vivo administration into cells a vector comprising and expressing the antisense cDNA which produces antisense mRNA which binds to native mRNA produced by a tubedown-1 gene, thereby inhibiting expression of said tubedown-1 protein.~~

Claim 27 is deleted:

~~27) The method of claim 26 wherein said method is used in combination with radiotherapy and other chemotherapeutic treatments.~~

Claim 28 is deleted:

~~28) A method for treatment of Ewing's Sarcoma family of tumors in a mammal, said method comprising administering to said mammal a safe and effective amount of an antisense cDNA derived from a cDNA molecule of SEQ ID NO. 2 sufficient to treat said condition.~~

Claim 29 is deleted:

~~29) The method of claim 28, wherein the antisense cDNA is selected from the group consisting of SEQ ID NO. 3 and SEQ ID NO. 4 and mixtures thereof.~~

Claim 30 is deleted:

~~30) The method of claim 29 wherein said method further comprises generation of the antisense oligonucleotide ex vivo which, when introduced into the cell, causes inhibition of expression of a tubedown-1 protein by hybridizing with mRNA and genomic sequences of a tbdn-1 gene.~~

Claim 31 is deleted:

~~31) The method of claim 30 wherein the antisense cDNA molecules are phosphoramidate, phosphothioate, methylphosphonate and other modified analogs of said cDNA molecules which are resistant to endogenous nucleases.~~

Claim 32 is deleted:

~~32) The method of claim 29 wherein said method further comprises providing the antisense cDNA's to cells of an individual expressing a tubedown-1 protein, said method comprising in vivo administration into cells a vector comprising and expressing the antisense cDNA's which produces antisense mRNA that binds to native mRNA produced by a tubedown-1 gene, thereby inhibiting expression of said tubedown-1 protein.~~

Claim 33 is deleted:

~~33) The method of claim 32 wherein said method is used in combination with radiotherapy and other chemotherapeutic treatments.~~

Claim 34 is deleted:

~~34) A method of inhibiting expression of a tubedown-1 protein in cells or tissues comprising contacting said cells or tissue in vitro with the antisense cDNA of claim 8 so that expression of said tbdn-1 protein is inhibited.~~

Claim 35 is deleted:

~~35) A method of inhibiting expression of a tubedown-1 protein in cells or tissues comprising contacting said cells or tissue in vitro with biological or chemical factors so that expression of said tbdn-1 protein is inhibited.~~

Claim 36 is deleted:

~~36) A replicable vector which comprises the antisense cDNA of claim 10.~~

Claim 37 is deleted:

~~37) A host cell which comprises the vector of claim 36.~~

Claim 38 is deleted:

~~38) The host cell of claim 37 wherein the host cell is a eukaryotic cell.~~

Claim 39 is deleted:

~~39) The host cell of claim 37 wherein the host cell is a bacterial cell.~~

Claim 40 is deleted:

~~40) The vector of claim 36 wherein the vector is a plasmid.~~

Claim 41 is deleted:

~~41) A single stranded antisense oligonucleotide derived from an antisense cDNA sequence of SEQ ID NO. 3 or 4, wherein the antisense oligonucleotide is at least 15 nucleobases in length and is of at least 70% complementarity to a native mRNA produced by a tubedown-1 gene.~~

Claim 42 is deleted:

~~42) The antisense oligonucleotide molecule of claim 41, wherein the antisense oligonucleotide and native mRNA hybridize under low and high stringency conditions.~~

Claim 43 is deleted:

~~43) A composition comprising a safe and effective amount of a single stranded antisense oligonucleotide at least 15 nucleobases in length derived from an antisense cDNA sequence of SEQ ID NO. 3 or 4, and a pharmaceutically acceptable carrier.~~

Claim 44 is deleted:

~~44) The composition of claim 43 wherein the antisense oligonucleotide is of at least 70% complementarity to mRNA produced by a native tubedown-1 gene.~~

Claim 45 is deleted:

~~45) The composition of claim 44 wherein the antisense oligonucleotide and native mRNA hybridize under low and high stringency conditions.~~

Claim 46 is deleted:

~~46) A method for treatment of osteosarcoma in a mammal, said method comprising administering to said mammal a safe and effective amount of a single stranded antisense oligonucleotide at least 15 nucleobases in length, derived from an antisense cDNA molecule of SEQ ID NO. 3 or 4, sufficient to treat said condition.~~

Claim 47 is deleted:

~~47) The method of claim 46 wherein the antisense oligonucleotides are phosphoramidate, phosphothioate, methylphosphonate and other modified analogs of said oligonucleotide which are resistant to endogenous nucleases.~~

Claim 48 is deleted:

~~48) The method of claim 47 wherein said method further comprises generation of the antisense oligonucleotide ex vivo which, when introduced into the cell, causes inhibition of expression of a tubedown 1 protein by hybridizing with mRNA and genomic sequences of a tbdn-1 gene.~~

Claim 49 is deleted:

~~49) A method for treatment of Ewing's Sarcoma family of tumors in a mammal, said method comprising administering to said mammal a safe and effective amount of a single stranded antisense oligonucleotide at least 15 nucleobases in length, derived from an antisense cDNA molecule of SEQ ID NO. 3 or 4, sufficient to treat said condition.~~

Claim 50 is added as follows:

**50. The isolated nucleic acid molecule of Claim 1, wherein said molecule is a single-stranded cDNA molecule.**

Claim 51 is added as follows:

**51. The isolated nucleic acid molecule of Claim 1, wherein said molecule is biologically active.**

Claim 52 is added as follows:

**52. The isolated nucleic acid molecule of claim 51, wherein said molecule or fragment thereof is used to generate a first antisense nucleic acid molecule of the sequence**

**shown in SEQ ID No. 2, wherein said first antisense nucleic acid molecule consists of the sequence shown in SEQ ID No. 3.**

Claim 53 is added as follows:

**53. The isolated first antisense nucleic acid molecule of Claim 52 consisting of the sequence shown in SEQ ID No. 3.**

Claim 54 is added as follows:

**54. The isolated first antisense nucleic acid molecule of Claim 53, wherein said first antisense molecule is a single-stranded, cDNA molecule.**

Claim 55 is added as follows:

**55. The isolated first antisense nucleic acid molecule of Claim 53, wherein said first antisense molecule is biologically active.**

Claim 56 is added as follows:

**56. The isolated first antisense nucleic acid molecule of Claim 55, wherein said first antisense molecule is capable of hybridizing with a native, genomic DNA molecule or fragment thereof encoding native, genomic tbdn-1 mRNA.**

Claim 57 is added as follows:

**57. The isolated first antisense nucleic acid molecule of Claim 55, wherein said first antisense molecule blocks transcription of said native, genomic DNA molecule or fragment thereof encoding native, genomic tbdn-1 mRNA into native, genomic tbdn-1 mRNA.**

Claim 58 is added as follows:

**58. The isolated first antisense nucleic acid molecule of Claim 55, wherein said first antisense molecule is capable of being transcribed into a first antisense tbdn-1 mRNA molecule that blocks translation of native, genomic tbdn-1 mRNA molecule or fragment thereof encoding tbdn-1 protein into tbdn-1 protein.**

Claim 59 is added as follows:

**59. The first antisense tbdn-1 mRNA molecule of Claim 58, wherein said first antisense mRNA molecule is a single-stranded oligonucleotide having at least 15 nucleobases.**

Claim 60 is added as follows:

**60. The first antisense tbdn-1 mRNA molecule of Claim 58, wherein said first antisense mRNA molecule is biologically active.**

Claim 61 is added as follows:

- 61. The first antisense tbdn-1 mRNA molecule of Claim 60, wherein said first antisense mRNA molecule is capable of hybridizing with native tbdn-1 mRNA molecule or fragment thereof encoding tbdn-1 protein.**

Claim 62 is added as follows:

- 62. The first antisense tbdn-1 mRNA molecule of Claim 60, wherein said first antisense mRNA molecule blocks translation of said native, genomic tbdn-1 mRNA molecule or fragment thereof encoding tbdn-1 protein into tbdn-1 protein.**

Claim 63 is added as follows:

- 63. The isolated nucleic acid molecule of claim 51, wherein said molecule or fragment thereof is used to generate a second antisense nucleic acid molecule of the sequence shown in SEQ ID No. 2, wherein said second antisense nucleic acid molecule consists of the sequence shown in SEQ ID No. 4.**

Claim 64 is added as follows:

- 64. The isolated second antisense nucleic acid molecule of Claim 63 consisting of the sequence shown in SEQ ID No. 4.**

Claim 65 is added as follows:

- 65. The isolated second antisense nucleic acid molecule of Claim 64, wherein said second antisense molecule is a single-stranded cDNA molecule.**

Claim 66 is added as follows:

- 66. The isolated second antisense nucleic acid molecule of Claim 64, wherein said second antisense molecule is biologically active.**

Claim 67 is added as follows:

- 67. The isolated second antisense nucleic acid molecule of Claim 66, wherein said second antisense molecule is capable of hybridizing with a native, genomic DNA molecule or fragment thereof encoding native, genomic tbdn-1 mRNA.**

Claim 68 is added as follows:

- 68. The isolated second antisense nucleic acid molecule of Claim 66, wherein said second antisense molecule blocks transcription of said native, genomic DNA molecule or fragment thereof encoding native, genomic tbdn-1 mRNA into native, genomic tbdn-1 mRNA.**

Claim 69 is added as follows:

**69. The isolated second antisense nucleic acid molecule of Claim 66, wherein said second antisense molecule is capable of being transcribed into a second antisense tbdn-1 mRNA molecule that blocks translation of native, genomic tbdn-1 mRNA molecule or fragment thereof encoding tbdn-1 protein into tbdn-1 protein.**

Claim 70 is added as follows:

**70. The second antisense tbdn-1 mRNA molecule of Claim 69, wherein said second antisense mRNA molecule is a single-stranded oligonucleotide having at least 15 nucleobases.**

Claim 71 is added as follows:

**71. The second antisense tbdn-1 mRNA molecule of Claim 69, wherein said second antisense mRNA molecule is biologically active.**

Claim 72 is added as follows:

**72. The second antisense tbdn-1 mRNA molecule of Claim 71, wherein said second antisense mRNA molecule is capable of hybridizing with native, genomic tbdn-1 mRNA molecule or fragment thereof encoding tbdn-1 protein.**

Claim 73 is added as follows:

**73. The second antisense tbdn-1 mRNA molecule of Claim 71, wherein said second antisense mRNA molecule blocks translation of said native, genomic tbdn-1 mRNA molecule or fragment thereof encoding tbdn-1 protein into tbdn-1 protein.**

Claim 74 is added as follows:

**74. A composition comprising the isolated first antisense nucleic acid molecule shown in SEQ ID No. 3 in an amount effective to limit the growth or metastasis of tumor cells expressing the tbdn-1 protein molecule when administered to said tumor cells.**

Claim 75 is added as follows:

**75. The composition of Claim 74, additionally comprising a vector selected from the group consisting of viral, plasmid, and mixtures thereof.**

Claim 76 is added as follows:

**76. The composition of Claim 74, wherein said tumor cells comprise Ewing's Sarcoma family of tumors or osteosarcoma tumors.**

Claim 77 is added as follows:

**77. A composition comprising the isolated second antisense nucleic acid molecule shown in SEQ ID No. 4 in an amount effective to limit the growth or metastasis of tumor cells expressing the tbdn-1 protein molecule when administered to said tumor cells.**

Claim 78 is added as follows:

**78. The composition of Claim 77, additionally comprising a vector selected from the group consisting of viral, plasmid, and mixtures thereof.**

Claim 79 is added as follows:

**79. The composition of Claim 77, wherein said tumor cells comprise Ewing's Sarcoma family of tumors or osteosarcoma tumors.**

Claim 80 is added as follows:

**80. A method for limiting the growth or metastasis of tumor cells expressing the tbdn-1 protein molecule comprising administering a therapeutically effective amount of the isolated first antisense nucleic acid molecule shown in SEQ ID No. 3 to said tumor cells to cause inhibition of the expression of tbdn-1 protein molecule by said tumor cells.**

Claim 81 is added as follows:

**81. The method of Claim 80, wherein said therapeutically effective amount of the isolated first antisense nucleic acid molecule shown in SEQ ID No. 3 comprises the composition of Claim 74.**

Claim 82 is added as follows:

**82. The method of Claim 80, wherein said therapeutically effective amount of the isolated first antisense nucleic acid molecule shown in SEQ ID No. 3 comprises the composition of Claim 75.**

Claim 83 is added as follows:

**83. The method of Claim 80, additionally comprising radiotherapy and chemotherapeutic agents.**

Claim 84 is added as follows:

**84. A method for limiting the growth or metastasis of tumor cells expressing the tbdn-1 protein molecule comprising administering a therapeutically effective amount of the isolated second antisense nucleic acid molecule shown in SEQ ID No. 4 to said tumor**



**cells to cause inhibition of the expression of tbdn-1 protein molecule by said tumor cells.**

Claim 85 is added as follows:

**85. The method of Claim 84, wherein said therapeutically effective amount of the isolated second antisense nucleic acid molecule shown in SEQ ID No. 4 comprises the composition of Claim 77.**

Claim 86 is added as follows:

**86. The method of Claim 84, wherein said therapeutically effective amount of the isolated second antisense nucleic acid molecule shown in SEQ ID No. 4 comprises the composition of Claim 78.**

Claim 87 is added as follows:

**87. The method of Claim 84, additionally comprising radiotherapy and chemotherapeutic agents.**